Tirzepatide: Drug information

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For additional information see "Tirzepatide: Patient drug information"

For abbreviations, symbols, and age group definitions show table

Special Alerts

Glucagon-Like Peptide-1 Receptor Agonists Safety Update January 2024

The FDA has been evaluating reports of suicidal thoughts or actions in patients treated with glucagon-like peptide-1 receptor agonists (GLP-1 RAs). A preliminary evaluation has not found evidence that the use of these medicines causes suicidal thoughts or actions, but the FDA is continuing to investigate this issue. Patients should not stop taking GLP-1 RAs without consulting their health care provider. Health care providers should monitor for and advise patients using GLP-1 RAs to report new or worsening depression, suicidal thoughts, or any unusual changes in mood or behavior.

Further information may be found at https://www.fda.gov/drugs/drug-safety-and-availability/update-fdas-ongoing-evaluation-reports-suicidal-thoughts-or-actions-patients-taking-certain-type.

ALERT: US Boxed Warning

Risk of thyroid C-cell tumors

In both male and female rats, tirzepatide causes dose-dependent and treatment-duration-dependent thyroid C-cell tumors at clinically relevant exposures. It is unknown whether tirzepatide causes thyroid C-cell tumors, including medullary thyroid carcinoma (MTC), in humans as human relevance of tirzepatide-induced rodent thyroid C-cell tumors has not been determined.

Tirzepatide is contraindicated in patients with a personal or family history of MTC or in patients with multiple endocrine neoplasia syndrome type 2 (MEN 2). Counsel patients regarding the potential risk for MTC with the use of tirzepatide and inform them of symptoms of thyroid tumors (eg, a mass in the neck, dysphagia, dyspnea, persistent hoarseness). Routine monitoring of serum calcitonin or using thyroid ultrasound is of uncertain value for early detection of MTC in patients treated with tirzepatide.

Brand Names: US

Mounjaro; Zepbound

Brand Names: Canada

Mounjaro; Mounjaro KwikPen; Zepbound KwikPen

Pharmacologic Category

Glucose-Dependent Insulinotropic Polypeptide (GIP)/Glucagon-Like Peptide (GLP-1) Receptor Agonist

Dosing: Adult

Dosage guidance:

Clinical considerations: Use is not recommended in patients with severe GI disease (eg, severe gastroparesis) (has not been studied).

Diabetes mellitus, type 2, treatment (Mounjaro):

Note: May be preferred in patients who would benefit from significant weight loss due to presence of weight-related comorbidities (eg, symptomatic heart failure with preserved ejection fraction, metabolic dysfunction associated steatohepatitis), and/or in patients with an HbA_{1c} relatively far from goal (eg, HbA_{1c} 9% to 10%) and type 1 diabetes is not likely (Ref). May require a dose reduction of insulin and/or insulin secretagogues (eg, sulfonylureas, meglitinides) to avoid hypoglycemia. Due to lack of additive glycemic benefit, avoid concomitant use with a dipeptidyl peptidase-4 inhibitor (Ref).

SUBQ: Initial: 2.5 mg once weekly for 4 weeks, then increase to 5 mg once weekly. May increase dose in 2.5 mg/week increments every 4 weeks if needed to achieve glycemic goals (maximum weekly dose: 15 mg/week). **Note:** The lower initial dose (2.5 mg weekly) is intended to reduce GI symptoms; it does not provide effective glycemic control. If changing the day of administration is necessary, allow at least 72 hours between 2 doses.

Weight management, chronic (Zepbound):

Note: For use as an adjunct to diet and exercise in patients with obesity, or in patients with overweight and ≥1 weight-related comorbidity (eg, cardiovascular disease, dyslipidemia, hypertension, obstructive sleep apnea, type 2 diabetes mellitus). Some experts favor use in individuals with highest risk of weight-related complications based on evaluation of BMI (eg, BMI ≥30 kg/m^2 or BMI 27 to 29.9 kg/m^2 plus at least one weight-related comorbidity) and waist circumference (Ref).

SUBQ: Initial: 2.5 mg once weekly for 4 weeks, then increase to 5 mg once weekly. May further increase dose in 2.5 mg/week increments every 4 weeks, if needed (maximum weekly dose: 15 mg/week). **Note:** The lower initial dose (2.5 mg weekly) is intended to reduce GI symptoms; it is not approved as a maintenance dose. If changing the day of administration is necessary, allow at least 72 hours between 2 doses.

Weight-related conditions, treatment (Zepbound):

Note: For use in patients with BMI ≥30 kg/m^2 and conditions that may improve with weight loss, including symptomatic heart failure with preserved ejection fraction (off label), metabolic dysfunction associated steatohepatitis (off label), and obstructive sleep apnea (labeled use) (Ref).

SUBQ: Initial: 2.5 mg once weekly for 4 weeks, then increase dose in 2.5 mg/week increments every 4 weeks to a recommended maintenance dose of 10 or 15 mg once weekly (maximum weekly dose: 15 mg/week) (Ref). **Note:** The lower initial dose (2.5 mg weekly) is intended to reduce GI symptoms; it is not approved as a maintenance dose for weight management. If changing the day of administration is necessary, allow at least 72 hours between 2 doses.

Missed doses:

Single missed dose: Administer missed dose as soon as possible within 4 days, then resume usual schedule thereafter. If >4 days have elapsed, skip the missed dose and resume administration at the next scheduled weekly dose.

Multiple missed doses: For patients on the 2.5 mg/week dose, reinitiate at 2.5 mg once weekly. For patients on doses ≥5 mg/week:

If 2 or fewer doses missed: Reinitiate at the same dose if previously tolerated (Ref).

If 3 or more doses missed: Reinitiate at 5 mg once weekly (Ref).

Dosage adjustment for concomitant therapy: Significant drug interactions exist, requiring dose/frequency adjustment or avoidance. Consult drug interactions database for more information.

Dosing: Kidney Impairment: Adult

No dosage adjustment necessary.

Dosing: Liver Impairment: Adult

No dosage adjustment necessary.

Dosing: Older Adult

Refer to adult dosing.

Adverse Reactions (Significant): Considerations

Acute kidney injury

Acute kidney injury (AKI), which sometimes requires dialysis, has been reported with glucagon-like peptide-1 (GLP-1) receptor agonists, including tirzepatide (Ref). According to the manufacturer, AKI occurred mostly in patients who experienced nausea, vomiting, diarrhea, or dehydration secondary to GLP-1 receptor agonists.

Mechanism: Non–dose-related; exact mechanism is unknown. Pre-renal AKI may occur due to dehydration and volume contraction secondary to GI symptoms (eg, nausea, vomiting, diarrhea) (Ref).

Onset: Varied; because the mechanism is thought to be related to volume contraction, timing may be dependent on GI symptoms, initiation or dosage adjustment of concurrent medications, and/or comorbid conditions (Ref).

Risk factors:

- Volume contraction (eg, during periods of severe vomiting or diarrhea) (Ref)
- Co-administration of medications known to result in kidney injury during episodes of dehydration (eg, drugs that inhibit the renin-angiotensin system) (Ref)
- Preexisting kidney impairment

Diabetic retinopathy

Diabetic retinopathy (DR) was reported with tirzepatide during the SURPASS-2 study, a clinical trial evaluating the safety and efficacy of tirzepatide compared to semaglutide in patients with type 2 diabetes (Ref); patients with a prior history of DR were excluded from this trial. In addition, rapid reductions in HbA_{1c} are associated with an early worsening of DR (Ref). In an analysis of DR complications due to the glucagon-like peptide-1 (GLP-1) receptor agonist semaglutide, the increased risk of DR was mainly observed in patients with preexisting DR and primarily attributable to the magnitude and rapidity of reduction in HbA_{1c} (Ref).

Mechanism: Unknown. In general, worsening of preexisting DR is a known consequence of rapid improvement of hyperglycemia, especially in patients with uncontrolled diabetes. Although unlikely, a direct toxic effect or potential angiogenic action of tirzepatide has not been ruled out (Ref).

Onset: Varied; clinicians should note that DR is a progressive condition, and the onset of DR complications may vary.

Risk factors:

- Preexisting DR
- In general, the risk of early worsening of DR is increased when intensive treatment is initiated in patient with long-standing poor glycemic control (Ref)

Gallbladder disease

Gallbladder disease and biliary tract disease, including **biliary colic**, **cholelithiasis**, **cholecystitis**, cholestasis, cholangitis, and **cholecystectomy** have been reported with glucagon-like peptide-1 (GLP-1) receptor agonists, including tirzepatide. Resolution of biliary stones following discontinuation has been documented with the GLP-receptor agonist liraglutide (Ref).

Mechanism: Dose- and time-related (Ref); not fully understood. Animal studies and in vitro data have demonstrated that GLP-1 enhances the proliferations and functional activity of cholangiocytes, which may result in gallbladder diseases (Ref). Some authors have postulated a change in bile acid production and secretion, suppressed secretion of cholecystokinin, decreased gallbladder emptying, prolonged gallbladder refilling, weight loss, or potentially a combination of these factors (Ref).

Onset: Varied; an increased risk was reported following >26 weeks of therapy (Ref).

Risk factors:

- Higher doses (Ref)
- Longer duration of treatment (eg, >26 weeks) (Ref)
- Substantial or rapid weight loss has been associated with an increased risk with GLP-1 receptor agonists used for weight loss (eg, liraglutide, semaglutide) (Ref)

Gastrointestinal symptoms

GI effects, including **abdominal pain**, **constipation**, **decreased appetite**, **diarrhea**, **dysgeusia**, **dyspepsia**, **nausea**, and **vomiting**, have been reported with tirzepatide (Ref). Symptoms may sometimes be severe. GI effects tend to occur during dose escalation and decrease over time; may result in treatment discontinuation.

Mechanism: Dose-related; however, the exact mechanism is not fully understood. May be a result of delayed gastric emptying or activation centers involved in appetite regulation, satiety, and nausea (Ref).

Onset: Intermediate; nausea, vomiting, and diarrhea are most common soon after initiation (eg, the first 4 weeks of treatment) and during dose escalation (Ref).

Risk factors:

- Dose; generally greater with higher doses
- In general, rapid titration of glucagon-like peptide-1 (GLP-1) receptor agonists is associated with higher risk of GI symptoms

Hypersensitivity reactions

Serious, immediate **hypersensitivity reactions**, including **anaphylaxis** and **angioedema**, have been reported with glucagon-like peptide-1 (GLP-1) receptor agonists, including tirzepatide. Delayed hypersensitivity reactions have also been documented with GLP-1 receptor agonists (Ref).

Mechanism: Non–dose-related; immunologic.

Immediate hypersensitivity reactions: IgE-antibodies are formed against a drug allergen following initial exposure (Ref).

Delayed hypersensitivity reactions: T-cell mediated (Ref).

Onset:

Immediate hypersensitivity reactions: Rapid; generally occurs within 1 hour of administration but may occur up to 6 hours after exposure (Ref)

Delayed hypersensitivity reactions: Varied; may occur from 1 day to 6 weeks after initiation (Ref).

Risk factors:

• Cross-reactivity between GLP-1 receptor agonists is unknown (Ref).

Hypoglycemia

Tirzepatide lowers blood glucose, which may result in **hypoglycemia** in patients with or without type 2 diabetes mellitus.

Mechanism: Related to the mechanism of action; glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist.

Risk factors:

• Concurrent insulin secretagogue (eg, sulfonylurea) and/or insulin

Medullary thyroid carcinoma

In the early stages of drug development, thyroid C-cell tumors were noted to have developed during animal studies with tirzepatide. It is unknown whether tirzepatide causes thyroid C-cell tumors in humans, as the human relevance of tirzepatide-induced rodent thyroid C-cell tumors has not been determined. Human cases of medullary thyroid carcinoma (MTC) have been reported with glucagon-like peptide-1 (GLP-1) receptor agonists dulaglutide and liraglutide (Ref).

Mechanism: Unknown; animal studies have shown dose-dependent and treatment duration-dependent harmful effects in rodents but not primates, thereby indicating that proliferative C-cell effects of GLP-1 receptor agonists may be rodent-specific. Humans have far fewer C-cells than rodents, and expression of the GLP-1 receptor in human C-cells is very low (Ref).

Risk factors:

• Patients with a personal or family history of MTC or patients with multiple endocrine neoplasia syndrome type 2 (MEN 2) may be at an increased risk

Pancreatitis

Cases of **acute pancreatitis** (including **hemorrhagic pancreatitis** and **necrotizing pancreatitis** with some fatalities), chronic pancreatitis, and pancreatic adenocarcinoma have been reported with use of incretin-based therapies (eg, dipeptidyl peptidase 4 inhibitors, glucagon-like peptide-1 [GLP-1] receptor agonists) (Ref). In clinical trials, acute pancreatitis was observed with tirzepatide.

Mechanism: Causality has not been firmly established (Ref). GLP-1 receptor agonists directly stimulate GLP-1 receptors in pancreatic islet beta cells and exocrine duct cells which may cause an overgrowth of the cells that cover the smaller ducts, thereby resulting in hyperplasia, increased pancreatic weight, duct occlusion, back pressure, and subsequent acute or chronic pancreatic inflammation (Ref).

Risk factors:

• Patients with a prior history of pancreatitis may be at an increased risk for acute pancreatitis

- Patients with acute pancreatitis due to any cause are at an increased risk for progression to recurrent acute pancreatitis and then to chronic pancreatitis; patients with chronic pancreatitis are at an increased risk for pancreatic cancer (Ref)
- Risk factors for pancreatitis due to any cause include, but are not limited to, hypertriglyceridemia, cholelithiasis, alcohol use, and obesity (Ref)

Adverse Reactions

The following adverse drug reactions and incidences are derived from product labeling unless otherwise specified. Adverse reactions reported in adults.

>10%:

Gastrointestinal: Constipation (6% to 17%) (table 1), decreased appetite (5% to 11%) (table 2), diarrhea (12% to 23%) (table 3), nausea (12% to 29%) (table 4), vomiting (5% to 13%) (table 5)

Tirzepatide: Adverse Reaction: Constipation

Drug (Tirzepatide)	Placebo	Dose	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)
17%	5%	5 mg once weekly	Obesity or overweight	630	958
14%	5%	10 mg once weekly	Obesity or overweight	948	958
11%	5%	15 mg once weekly	Obesity or overweight	941	958
7%	1%	15 mg once weekly	Type 2 diabetes mellitus	241	235
6%	1%	10 mg once weekly	Type 2 diabetes mellitus	240	235
6%	1%	5 mg once weekly	Type 2 diabetes mellitus	237	235

Tirzepatide: Adverse Reaction: Decreased Appetite

Drug (Tirzepatide)	Placebo	Dose	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)
11%	1%	15 mg once weekly	Type 2 diabetes mellitus	241	235
10%	1%	10 mg once weekly	Type 2 diabetes mellitus	240	235
5%	1%	5 mg once weekly	Type 2 diabetes mellitus	237	235

Tirzepatide: Adverse Reaction: Diarrhea

Drug (Tirzepatide)	Placebo	Dose	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)
23%	8%	15 mg once weekly	Obesity or overweight	941	958
21%	8%	10 mg once weekly	Obesity or overweight	948	958
19%	8%	5 mg once weekly	Obesity or overweight	630	958
17%	9%	15 mg once weekly	Type 2 diabetes mellitus	241	235
13%	9%	10 mg once weekly	Type 2 diabetes mellitus	240	235
12%	9%	5 mg once weekly	Type 2 diabetes mellitus	237	235

Tirzepatide: Adverse Reaction: Nausea

Drug (Tirzepatide)	Placebo	Dose	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)
29%	8%	10 mg once weekly	Obesity or overweight	948	958
28%	8%	15 mg once weekly	Obesity or overweight	941	958
25%	8%	5 mg once weekly	Obesity or overweight	630	958
18%	4%	15 mg once weekly	Type 2 diabetes mellitus	241	235
15%	4%	10 mg once weekly	Type 2 diabetes mellitus	240	235
12%	4%	5 mg once weekly	Type 2 diabetes mellitus	237	235

Tirzepatide: Adverse Reaction: Vomiting

Drug (Tirzepatide)	Placebo	Dose	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)

Drug (Tirzepatide)	Placebo	Dose	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)
13%	2%	15 mg once weekly	Obesity or overweight	941	958
11%	2%	10 mg once weekly	Obesity or overweight	948	958
8%	2%	5 mg once weekly	Obesity or overweight	630	958
9%	2%	15 mg once weekly	Type 2 diabetes mellitus	241	235
5%	2%	10 mg once weekly	Type 2 diabetes mellitus	240	235
5%	2%	5 mg once weekly	Type 2 diabetes mellitus	237	235

Immunologic: Antibody development (51% to 65%; neutralizing: ≤3%)

1% to 10%:

Cardiovascular: Hypotension (1% to 2%), sinus tachycardia (5% to 10%) (table 6)

Tirzepatide: Adverse Reaction: Sinus Tachycardia

Drug (Tirzepatide)	Placebo	Dose	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)	Comments
10%	4%	15 mg once weekly	Type 2 diabetes mellitus	241	235	Increase from baseline in heart rate of ≥15 beats per minute
6%	4%	10 mg once weekly	Type 2 diabetes mellitus	240	235	Increase from baseline in heart rate of ≥15 beats per minute
5%	4%	5 mg once weekly	Type 2 diabetes mellitus	237	235	Increase from baseline in heart rate of ≥15 beats per minute

Dermatologic: Alopecia (4% to 5%; more common in females)

Endocrine & metabolic: Hypoglycemia (0.3% to 4%) (table 7)

Tirzepatide: Adverse Reaction: Hypoglycemia

Drug (Tirzepatide)	Placebo	Population	Indication	Comments

Drug (Tirzepatide)	Placebo	Population	Indication	Comments
4%	1%	Patients with type 2 diabetes mellitus and BMI ≥ 27 kg/m^2	Obesity or overweight	Plasma glucose <54 mg/dL. Rates increased with combination hypoglycemia agents.
0.3%	0%	Patients with obesity/overweight (without type 2 diabetes mellitus)	Obesity or overweight	Plasma glucose <54 mg/dL.

Gastrointestinal: Abdominal distention (3% to 4%), abdominal pain (5% to 10%) (table 8), dyspepsia (5% to 10%) (table 9), eructation (3% to 5%), flatulence (1% to 4%), gallbladder disease (acute; including biliary colic, cholecystectomy [0.2%] (table 10), cholecystitis [0.2%] (table 11), cholelithiasis [0.6% to 1%] (table 12)), gastroesophageal reflux disease (2% to 5%)

Tirzepatide: Adverse Reaction: Abdominal Pain

Drug (Tirzepatide)	Placebo	Dose	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)
10%	5%	15 mg once weekly	Obesity or overweight	941	958
9%	5%	10 mg once weekly	Obesity or overweight	948	958
9%	5%	5 mg once weekly	Obesity or overweight	630	958
6%	4%	5 mg once weekly	Type 2 diabetes mellitus	237	235
5%	4%	15 mg once weekly	Type 2 diabetes mellitus	241	235
5%	4%	10 mg once weekly	Type 2 diabetes mellitus	240	235

Tirzepatide: Adverse Reaction: Cholecystectomy

Drug (Tirzepatide)	Placebo	Indication
0.2%	0%	Obesity or overweight

Tirzepatide: Adverse Reaction: Cholecystitis

Drug (Tirzepatide)	Placebo	Indication
0.7%	0.2%	Obesity or overweight

Tirzepatide: Adverse Reaction: Cholelithiasis

Drug (Tirzepatide)	Placebo	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)
1%	1%	Obesity or overweight	N/A	N/A
0.6%	0%	Type 2 diabetes mellitus	718	235

Tirzepatide: Adverse Reaction: Dyspepsia

Drug (Tirzepatide)	Placebo	Dose	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)
10%	4%	15 mg once weekly	Obesity or overweight	941	958
9%	4%	10 mg once weekly	Obesity or overweight	948	958
9%	4%	5 mg once weekly	Obesity or overweight	630	958
8%	3%	5 mg once weekly	Type 2 diabetes mellitus	237	235
8%	3%	10 mg once weekly	Type 2 diabetes mellitus	240	235
5%	3%	15 mg once weekly	Type 2 diabetes mellitus	241	235

Hypersensitivity: Hypersensitivity reaction (2% to 5%; including severe hypersensitivity reaction [<1%]) (table 13)

Tirzepatide: Adverse Reaction: Hypersensitivity Reaction

Drug (Tirzepatide)	Placebo	Dose	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)	Comments
5%	3%	15 mg once weekly	Obesity or overweight	941	958	N/A
5%	3%	10 mg once weekly	Obesity or overweight	948	958	N/A
5%	3%	5 mg once weekly	Obesity or overweight	630	958	N/A
4%	3%	N/A	Obesity or overweight	N/A	N/A	Delayed reaction

Drug (Tirzepatide)	Placebo	Dose	Indication	Number of Patients (Tirzepatide)	Number of Patients (Placebo)	Comments
2%	0.4%	N/A	Obesity or overweight	N/A	N/A	Immediate reaction
3%	2%	N/A	Type 2 diabetes mellitus	718	235	N/A

Local: Injection-site reaction (3% to 8%)

Nervous system: Dizziness (4% to 5%), fatigue (5% to 7%)

Respiratory: Dry throat (1%)

<1%:

Gastrointestinal: Dysgeusia

Nervous system: Dysesthesia

Frequency not defined: Gastrointestinal: Delayed gastric emptying

Postmarketing:

Endocrine & metabolic: Diabetic retinopathy (Ref)

Gastrointestinal: Acute pancreatitis (including hemorrhagic pancreatitis, necrotizing pancreatitis) (Ref), gastric outlet obstruction (Ref), increased serum amylase (Ref), increase serum lipase (Ref), intestinal obstruction

Hepatic: Hepatotoxicity (Ref)

Hypersensitivity: Anaphylaxis, angioedema

Renal: Acute kidney injury (Ref), exacerbation of renal failure

Contraindications

Serious hypersensitivity to tirzepatide or any component of the formulation; serious hypersensitivity reactions including anaphylaxis and angioedema have been reported; a personal or family history of medullary thyroid carcinoma or in patients with multiple endocrine neoplasia syndrome type 2 (MEN 2).

Canadian labeling: Additional contraindications (not in US labeling): Breastfeeding; pregnancy.

Warnings/Precautions

Disease-related concerns:

• Bariatric surgery:

- Dehydration: Evaluate, correct, and maintain postsurgical fluid requirements and volume status prior to initiating therapy, and closely monitor the patient for the duration of therapy; acute and chronic kidney failure exacerbation may occur. A majority of cases occurred in patients with nausea, vomiting, diarrhea, and/or dehydration. Nausea is common and fluid intake may be more difficult after gastric bypass, sleeve gastrectomy, and gastric band (Mechanick 2020).

- Excessive glucagon-like peptide-1 exposure: Closely monitor for efficacy and assess for signs and symptoms of pancreatitis if therapy is initiated after surgery; gastric bypass and sleeve gastrectomy (but not gastric band) significantly increase endogenous postprandial GLP-1 concentrations (Korner 2009; Peterli 2012). Administration of exogenous GLP-1 receptor agonists may be redundant to surgery effects.

Concurrent drug therapy issues:

- Delayed gastric emptying: Tirzepatide slows gastric emptying, which may alter the absorption of other medications. Monitor narrow therapeutic index medications for increased or decreased response.

Other warnings/precautions:

- Appropriate use: Diabetes mellitus: Do not use in patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis; not a substitute for insulin.

- Surgical and endoscopic procedures: Use of glucagon-like peptide-1 receptor agonists (GLP-1 RAs) has been associated with elevated residual gastric contents, which may increase the risk for adverse events during anesthesia and deep sedation (including aspiration) (Kobori 2023; Marroquin-Harris 2023; Silveira 2023). In some studies, delayed gastric emptying induced by GLP-1 RAs returned to baseline after 8 to 12 weeks of continuous therapy; therefore, risk may be higher in patients who recently initiated therapy or who use GLP-1 RAs intermittently (Raven 2024; van Zuylen 2024). Although the American Society of Anesthesiologists has suggested holding GLP-1 RAs prior to planned procedures requiring general anesthesia, the risks and benefits of this approach have not been evaluated (AGA [Hashash 2023]; ASA [Joshi 2023]). For example, in patients using GLP-1 RAs for glycemic control, holding the medication may result in perioperative hyperglycemia and increase the risk of adverse postoperative outcomes (AGA [Hashash 2023]; van Zuylen 2024). Individualize the decision to hold the GLP-1 RA based on patient-specific factors such as the indication (eg, glycemic control vs weight management), duration and frequency of therapy, presence of adverse GI symptoms, and concomitant medications that may slow gastric emptying (eg, opioids, proton pump inhibitors); may consider additional preoperative interventions (eg, clear liquid diet, full stomach precautions, gastric ultrasound) on a case-by-case basis to reduce risk (ASA [Hashash 2023]; Marroquin-Harris 2023; Raven 2024; van Zuylen 2024). Refer also to institutional protocols.

Dosage Forms: US

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Subcutaneous [preservative free]:

Zepbound: 2.5 mg/0.5 mL (0.5 mL); 5 mg/0.5 mL (0.5 mL); 7.5 mg/0.5 mL (0.5 mL); 10 mg/0.5 mL (0.5 mL); 12.5 mg/0.5 mL (0.5 mL); 15 mg/0.5 mL (0.5 mL)

Solution Auto-injector, Subcutaneous [preservative free]:

Mounjaro: 2.5 mg/0.5 mL (0.5 mL); 5 mg/0.5 mL (0.5 mL); 7.5 mg/0.5 mL (0.5 mL); 10 mg/0.5 mL (0.5 mL); 12.5 mg/0.5 mL (0.5 mL); 15 mg/0.5 mL (0.5 mL)

Zepbound: 2.5 mg/0.5 mL (0.5 mL); 5 mg/0.5 mL (0.5 mL); 7.5 mg/0.5 mL (0.5 mL); 10 mg/0.5 mL (0.5 mL); 12.5 mg/0.5 mL (0.5 mL); 15 mg/0.5 mL (0.5 mL)

Generic Equivalent Available: US

No

Pricing: US

Solution (Zepbound Subcutaneous)

2.5 mg/0.5 mL (per 0.5 mL): $104.70

5 mg/0.5 mL (per 0.5 mL): $149.70

7.5 mg/0.5 mL (per 0.5 mL): $179.70

10 mg/0.5 mL (per 0.5 mL): $209.70

12.5 mg/0.5 mL (per 0.5 mL): $254.70

15 mg/0.5 mL (per 0.5 mL): $314.70

Solution Auto-injector (Mounjaro Subcutaneous)

2.5 mg/0.5 mL (per 0.5 mL): $323.93

5 mg/0.5 mL (per 0.5 mL): $323.93

7.5 mg/0.5 mL (per 0.5 mL): $323.93

10 mg/0.5 mL (per 0.5 mL): $323.93

12.5 mg/0.5 mL (per 0.5 mL): $323.93

15 mg/0.5 mL (per 0.5 mL): $323.93

Solution Auto-injector (Zepbound Subcutaneous)

2.5 mg/0.5 mL (per 0.5 mL): $325.91

5 mg/0.5 mL (per 0.5 mL): $325.91

7.5 mg/0.5 mL (per 0.5 mL): $325.91

10 mg/0.5 mL (per 0.5 mL): $325.91

12.5 mg/0.5 mL (per 0.5 mL): $325.91

15 mg/0.5 mL (per 0.5 mL): $325.91

Disclaimer: A representative AWP (Average Wholesale Price) price or price range is provided as reference price only. A range is provided when more than one manufacturer's AWP price is available and uses the low and high price reported by the manufacturers to determine the range. The pricing data should be used for benchmarking purposes only, and as such should not be used alone to set or adjudicate any prices for reimbursement or purchasing functions or considered to be an exact price for a single product and/or manufacturer. Medi-Span expressly disclaims all warranties of any kind or nature, whether express or implied, and assumes no liability with respect to accuracy of price or price range data published in its solutions. In no event shall Medi-Span be liable for special, indirect, incidental, or consequential damages arising from use of price or price range data. Pricing data is updated monthly.

Dosage Forms: Canada

Excipient information presented when available (limited, particularly for generics); consult specific product labeling.

Solution, Subcutaneous:

Mounjaro: 2.5 mg/0.5 mL (0.5 mL); 5 mg/0.5 mL (0.5 mL); 7.5 mg/0.5 mL (0.5 mL); 10 mg/0.5 mL (0.5 mL); 12.5 mg/0.5 mL (0.5 mL); 15 mg/0.5 mL (0.5 mL)

Solution Auto-injector, Subcutaneous:

Mounjaro: 2.5 mg/0.5 mL (0.5 mL); 5 mg/0.5 mL (0.5 mL); 7.5 mg/0.5 mL (0.5 mL); 10 mg/0.5 mL (0.5 mL); 12.5 mg/0.5 mL (0.5 mL); 15 mg/0.5 mL (0.5 mL)

Solution Pen-injector, Subcutaneous:

Mounjaro KwikPen: 2.5 mg/0.6 mL (2.4 mL); 5 mg/0.6 mL (2.4 mL); 7.5 mg/0.6 mL (2.4 mL); 10 mg/0.6 mL (2.4 mL); 12.5 mg/0.6 mL (2.4 mL); 15 mg/0.6 mL (2.4 mL) [contains benzyl alcohol, phenol]

Zepbound KwikPen: 2.5 mg/0.6 mL (2.4 mL); 5 mg/0.6 mL (2.4 mL); 7.5 mg/0.6 mL (2.4 mL); 10 mg/0.6 mL (2.4 mL); 12.5 mg/0.6 mL (2.4 mL); 15 mg/0.6 mL (2.4 mL) [contains benzyl alcohol, phenol]

Administration: Adult

SUBQ: Administer by SUBQ injection into the abdomen, thigh, or upper arm at any time of day on the same day each week, with or without food. If changing the day of administration is necessary, allow ≥72 hours between 2 doses. Rotate injection sites with each dose. When using the single-dose vial use a syringe appropriate for dose administration (eg, a 1 mL syringe for measuring a 0.5 mL dose). Do not mix with other injectable products (eg, insulin); administer as separate injections. Avoid adjacent injections if administering other agents in the same area of the body. Solution should be clear and colorless to slightly yellow; do not use if particulate matter or discoloration are seen. Do not inject into skin that has lumps or pits or skin that is bruised, damaged, hard, scaly, scarred, tender, or thickened.

Mounjaro and Zepbound single-dose pens **do not** require priming before injection. For the Mounjaro Kwikpen and Zepbound Kwikpen multidose pens (Canadian products), prime the needle before injecting by turning the dose selector 2 clicks to the prime indicator and injecting into the air. Use a new needle for each injection. Once injected into the body, continue to depress the button until the dial has returned to 0 **and** for an additional 5 seconds. Then, remove the needle.

Medication Guide and/or Vaccine Information Statement (VIS)

An FDA-approved patient medication guide, which is available with the product information and as follows, must be dispensed with this medication:

Mounjaro: https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/215866s002s006lbl.pdf#page=20

Use: Labeled Indications

Type 2 diabetes mellitus, treatment (Mounjaro): As an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus.

Limitations of use: Has not been studied in patients with a history of pancreatitis; not indicated for use in patients with type 1 diabetes mellitus.

Obstructive sleep apnea, moderate to severe (Zepbound): Treatment of moderate to severe obstructive sleep apnea in adults with obesity.

Weight management, chronic (Zepbound): As an adjunct to a reduced-calorie diet and increased physical activity to reduce excess body weight and maintain weight reduction long-term in adults with obesity, or in adults with overweight in the presence of ≥1 weight-related comorbid condition (eg, cardiovascular disease, dyslipidemia, hypertension, obstructive sleep apnea, type 2 diabetes mellitus).

Use: Off-Label: Adult

Heart failure with preserved ejection fraction, weight management; Metabolic dysfunction–associated steatohepatitis, weight management

Medication Safety Issues

Sound-alike/look-alike issues:

Tirzepatide may be confused with teriparatide, tolazamide.

Mounjaro may be confused with Monjuvi.

Metabolism/Transport Effects

None known.

Drug Interactions

(For additional information: Launch drug interactions program)

Note: Interacting drugs may **not be individually listed below** if they are part of a group interaction (eg, individual drugs within "CYP3A4 Inducers [Strong]" are NOT listed). For a complete list of drug interactions by individual drug name and detailed management recommendations, use the drug interactions program by clicking on the "Launch drug interactions program" link above.

Alectinib: Glucagon-Like Peptide-1 Agonists may decrease serum concentrations of Alectinib. *Risk C: Monitor*

Alpha-Lipoic Acid: May increase hypoglycemic effects of Antidiabetic Agents. *Risk C: Monitor*

Androgens: May increase hypoglycemic effects of Agents with Blood Glucose Lowering Effects. *Risk C: Monitor*

Beta-Blockers (Beta1 Selective): May increase adverse/toxic effects of Antidiabetic Agents. Specifically, beta-blockers may mask the hypoglycemic symptoms of antidiabetic agents. *Risk C: Monitor*

Beta-Blockers (Nonselective): May increase hypoglycemic effects of Antidiabetic Agents. Beta-Blockers (Nonselective) may increase adverse/toxic effects of Antidiabetic Agents. Specifically, beta-blockers may mask the hypoglycemic symptoms of antidiabetic agents. *Risk C: Monitor*

Bortezomib: May increase therapeutic effects of Antidiabetic Agents. Bortezomib may decrease therapeutic effects of Antidiabetic Agents. *Risk C: Monitor*

Direct Acting Antiviral Agents (HCV): May increase hypoglycemic effects of Antidiabetic Agents. *Risk C: Monitor*

Etilefrine: May decrease therapeutic effects of Antidiabetic Agents. *Risk C: Monitor*

Glucagon-Like Peptide-1 Agonists: Tirzepatide may increase adverse/toxic effects of Glucagon-Like Peptide-1 Agonists. *Risk X: Avoid*

Guanethidine: May increase hypoglycemic effects of Antidiabetic Agents. *Risk C: Monitor*

Hormonal Contraceptives: Tirzepatide may decrease serum concentrations of Hormonal Contraceptives. Management: Patients using oral hormonal contraceptives should switch to a non-oral contraceptive method, or add a barrier method of contraception, for 4 weeks after initiation of tirzepatide and for 4 weeks after each dose escalation of tirzepatide. *Risk D: Consider Therapy Modification*

Hyperglycemia-Associated Agents: May decrease therapeutic effects of Antidiabetic Agents. *Risk C: Monitor*

Hypoglycemia-Associated Agents: Antidiabetic Agents may increase hypoglycemic effects of Hypoglycemia-Associated Agents. *Risk C: Monitor*

Insulin: Glucagon-Like Peptide-1 Agonists may increase hypoglycemic effects of Insulin. Management: Consider insulin dose reductions when used in combination with glucagon-like peptide-1 agonists. Monitor patients for hypoglycemia. *Risk D: Consider Therapy Modification*

Liraglutide: May increase adverse/toxic effects of Glucagon-Like Peptide-1 Agonists. *Risk X: Avoid*

Maitake: May increase hypoglycemic effects of Agents with Blood Glucose Lowering Effects. *Risk C: Monitor*

Meglitinides: Glucagon-Like Peptide-1 Agonists may increase hypoglycemic effects of Meglitinides. Management: Consider meglitinide dose reductions when used in combination with glucagon-like peptide-1 agonists, particularly when also used with basal insulin. *Risk D: Consider Therapy Modification*

Monoamine Oxidase Inhibitors: May increase hypoglycemic effects of Agents with Blood Glucose Lowering Effects. *Risk C: Monitor*

Pegvisomant: May increase hypoglycemic effects of Agents with Blood Glucose Lowering Effects. *Risk C: Monitor*

Prothionamide: May increase hypoglycemic effects of Agents with Blood Glucose Lowering Effects. *Risk C: Monitor*

Quinolones: May increase hypoglycemic effects of Agents with Blood Glucose Lowering Effects. Quinolones may decrease therapeutic effects of Agents with Blood Glucose Lowering Effects. Specifically, if an agent is being used to treat diabetes, loss of blood sugar control may occur with quinolone use. *Risk C: Monitor*

Reproterol: May decrease therapeutic effects of Antidiabetic Agents. *Risk C: Monitor*

Ritodrine: May decrease therapeutic effects of Antidiabetic Agents. *Risk C: Monitor*

Salicylates: May increase hypoglycemic effects of Agents with Blood Glucose Lowering Effects. *Risk C: Monitor*

Selective Serotonin Reuptake Inhibitor: May increase hypoglycemic effects of Agents with Blood Glucose Lowering Effects. *Risk C: Monitor*

Semaglutide: May increase adverse/toxic effects of Glucagon-Like Peptide-1 Agonists. *Risk X: Avoid*

Sincalide: Drugs that Affect Gallbladder Function may decrease therapeutic effects of Sincalide. Management: Consider discontinuing drugs that may affect gallbladder motility prior to the use of sincalide to stimulate gallbladder contraction. *Risk D: Consider Therapy Modification*

Sulfonylureas: Glucagon-Like Peptide-1 Agonists may increase hypoglycemic effects of Sulfonylureas. Management: Consider sulfonylurea dose reductions when used in combination with glucagon-like peptide-1 agonists. *Risk D: Consider Therapy Modification*

Thiazide and Thiazide-Like Diuretics: May decrease therapeutic effects of Antidiabetic Agents. *Risk C: Monitor*

Warfarin: Tirzepatide may increase serum concentrations of Warfarin. Tirzepatide may decrease serum concentrations of Warfarin. *Risk C: Monitor*

Reproductive Considerations

Agents other than tirzepatide are currently recommended for patients with type 2 diabetes mellitus planning to become pregnant (ADA 2025).

Obesity increases the risk of infertility. Optimal weight control prior to conception improves pregnancy outcomes; however, medications for weight loss are not recommended prior to pregnancy due to safety issues and adverse events. Weight loss medications should be discontinued prior to conception (ACOG 2021; Wharton 2020).

Tirzepatide may decrease the efficacy of oral hormonal contraception due to changes in gastric emptying; contraceptives administered by a nonoral route are not affected. Because the changes in gastric emptying are largest following the first dose, patients using an oral contraceptive should add a barrier method for 4 weeks after starting tirzepatide treatment and for 4 weeks after each dose increase. Alternately, patients can be switched to nonoral contraceptive methods.

Consult drug interactions database for more detailed information specific to use of tirzepatide and specific contraceptives.

Pregnancy Considerations

Based on data from animal reproduction studies, in utero exposure to tirzepatide may cause fetal harm.

Poorly controlled diabetes during pregnancy can be associated with an increased risk of adverse maternal and fetal outcomes, including diabetic ketoacidosis, preeclampsia, spontaneous abortion, preterm delivery, delivery complications, major malformations, stillbirth, and macrosomia (ACOG 2018). To prevent adverse outcomes, prior to conception and throughout pregnancy, maternal blood glucose and HbA_{1c} should be kept as close to target goals as possible but without causing significant hypoglycemia (ADA 2025).

Agents other than tirzepatide are currently recommended to treat diabetes mellitus in pregnancy (ADA 2025).

An increased risk of adverse maternal and fetal events is associated with obesity; however, moderate gestational weight gain based on prepregnancy BMI is required for positive fetal outcomes in all pregnancies, including patients who are overweight or obese. Therefore, medications for weight loss therapy are not recommended during pregnancy (ACOG 2021; Wharton 2020). Patients should discontinue tirzepatide once pregnancy is recognized.

Data collection to monitor pregnancy and infant outcomes following exposure to tirzepatide is ongoing. Health care providers are encouraged to enroll patients exposed to Zepbound during pregnancy in the registry (1-800-545-5979); patients may also enroll themselves.

Breastfeeding Considerations

It is not known if tirzepatide is present in breast milk.

According to the manufacturer, the decision to breastfeed during therapy should consider the risk of infant exposure, the benefits of breastfeeding to the infant, and the benefits of treatment to the mother.

Monitoring Parameters

Plasma glucose; GI adverse reactions (eg, nausea, vomiting, diarrhea); kidney function (at baseline and following dose increases in patients with kidney impairment reporting severe GI adverse reactions); signs/symptoms of pancreatitis (eg, persistent severe abdominal pain, which may radiate to the back and that may or may not be accompanied by vomiting); signs/symptoms of gallbladder disease; worsening of diabetic retinopathy (particularly in those with a prior history of the disease); emergence of worsening depression, suicidal thoughts/behavior, changes in behavior; heart rate; body weight (when used for chronic weight management).

HbA_{1c}: Monitor at least twice yearly in patients who have stable glycemic control and are meeting treatment goals; monitor quarterly in patients in whom treatment goals have not been met, or with therapy change. **Note:** In patients prone to glycemic variability (eg, patients with insulin deficiency), or in patients whose HbA_{1c} is discordant with serum glucose levels or

symptoms, consider evaluating HbA_{1c} in combination with blood glucose levels and/or a glucose management indicator (ADA 2025; KDIGO 2020).

Reference Range

Recommendations for glycemic control in patients with diabetes:

Nonpregnant adults (AACE [Samson 2023], ADA 2025):

HbA_{1c}: <7% (a more aggressive [<6.5%] or less aggressive [<8%] HbA_{1c} goal may be targeted based on patient-specific characteristics). **Note:** In patients using a continuous glucose monitoring system, a goal of time in range >70% with time below range <4% is recommended and is similar to a goal HbA_{1c} <7%.

Preprandial capillary blood glucose: 80 to 130 mg/dL (SI: 4.4 to 7.2 mmol/L) (more or less stringent goals may be appropriate based on patient-specific characteristics).

Peak postprandial capillary blood glucose (~1 to 2 hours after a meal): <180 mg/dL (SI: <10 mmol/L) (more or less stringent goals may be appropriate based on patient-specific characteristics).

Older adults (≥65 years of age) (ADA 2025):

Note: Consider less strict targets in patients who are using insulin and/or insulin secretagogues (sulfonylureas, meglitinides) (ES [LeRoith 2019]).

HbA_{1c}: <7% to 7.5% (healthy); <8% (complex/intermediate health). **Note:** Individualization may be appropriate based on patient and caregiver preferences and/or presence of cognitive impairment. In patients with very complex or poor health (ie, limited remaining life expectancy), consider making therapy decisions based on avoidance of hypoglycemia and symptomatic hyperglycemia rather than HbA_{1c} level.

Preprandial capillary blood glucose: 80 to 130 mg/dL (SI: 4.4 to 7.2 mmol/L) (healthy); 90 to 150 mg/dL (SI: 5 to 8.3 mmol/L) (complex/intermediate health); 100 to 180 mg/dL (SI: 5.6 to 10 mmol/L) (very complex/poor health).

Bedtime capillary blood glucose: 80 to 180 mg/dL (SI: 4.4 to 10 mmol/L) (healthy); 100 to 180 mg/dL (SI: 5.6 to 10 mmol/L) (complex/intermediate health); 110 to 200 mg/dL (SI: 6.1 to 11.1 mmol/L) (very complex/poor health).

Classification of hypoglycemia (ADA 2025):

Level 1: 54 to 70 mg/dL (SI: 3 to 3.9 mmol/L); hypoglycemia alert value; initiate fast-acting carbohydrate (eg, glucose) treatment.

Level 2: <54 mg/dL (SI: <3 mmol/L); threshold for neuroglycopenic symptoms; requires immediate action.

Level 3: Hypoglycemia associated with a severe event characterized by altered mental and/or physical status requiring assistance.

Mechanism of Action

Tirzepatide is a glucose-dependent insulinotropic polypeptide (GIP) receptor and glucagon-like peptide-1 (GLP-1) receptor agonist that increases glucose-dependent insulin secretion, decreases inappropriate glucagon secretion, slows gastric emptying, and decreases food intake (likely due to appetite mediation).

Pharmacokinetics (Adult Data Unless Noted)

Distribution: V_{dss}: ~9.7 to 11.8 L.

Protein binding: 99% to plasma albumin.

Metabolism: By proteolytic cleavage of the peptide backbone, beta-oxidation of the C20 fatty diacid moiety, and amide hydrolysis.

Bioavailability: 80%.

Half-life elimination: ~5 days.

Time to peak: 8 to 72 hours.

Excretion: Urine and feces (as metabolites).

Clearance: 0.056 to 0.061 L/hour.

Brand Names: International

For country code abbreviations (show table)

(QA) Qatar: Mounjaro | Mounjaro KwikPen

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